

Claims 1-6 are rejected under 35 USC § 102(e) as being anticipated by U.S. Patent No. 5,905,149 to Battistini et al. (hereinafter Battistini '149 ). This rejection is respectfully traversed for at least the following reasons.

Battistini et al. are concerned with a new class of tyrosine kinase inhibitors. No examples are provided of tablets containing one or more dry binders but no preswollen starch. In fact the only Example that contains starch explicitly states that pre-swollen starch is present in the composition. See Example 17 of Battistini et al. disclosing: "corn starch (10g) is suspended in warm water (90 ml) and the resulting paste is used to granulate the powder" (col. 18, lines 47-49). Thus, the teaching of Battistini does not disclose each and every limitation of the present invention.

The Examiner further states that "Regarding to claims 4-6, it is the position of the Examiner that no criticality is seen in the amounts of the ingredients since the reference obtains the same results desire [sic] by the applicants." This statement by the Examiner is not appropriate for an anticipation rejection under the statutory provisions of 35 U.S.C. 102. In order to anticipate the claimed invention, Battistini et al. must teach all of the limitations of the claims. It is immaterial for the anticipation rejection whether applicants have shown any criticality of the ranges. The claimed ranges must be disclosed by the reference. The Examiner, on page 3, in the rejection under 35 U.S.C. 103 states that Battistini et al 'is silent as to the teachings of the amounts of the ingredients." Because the reference does not teach the negative limitation explicitly recited in the claims, or the claimed limitations of the components, Applicants submit that the claimed invention is not anticipated by Battistini et al. Therefore, Applicants respectfully request that the Section 102-based rejection be withdrawn.

For these reasons, it is respectfully submitted that the present invention is not anticipated by Battistini et al. Reconsideration and withdrawal of the rejection are respectfully requested.

Claims 1-4<sup>P</sup> were rejected under 35 USC § 103 as being unpatentable over U.S. Patent No. 5,905,149 to Battistini et al. (hereinafter Battistini '149 ) in view of U.S. Patent No. 5,593,691 to Eugster et al. (hereinafter Eugster '691). Applicants traverse this rejection for at least the following reasons.

As discussed above, Battistini '149 expressly teaches that preswollen starch is an acceptable binder. The cornstarch described in Example 17 of Battistini '149 is a preswollen corn starch: "corn starch (10g) is suspended in warm water (90 ml) and the resulting paste is used to granulate the powder" (col. 18, lines 47-49). Therefore, Battistini '149 teaches away from the claimed invention which explicitly excludes preswollen starch. Furthermore, the Battistini reference does not disclose the claimed amounts of the components. The Examiner cites Eugster to overcome the deficiencies of Battistini '149. Eugster '691 teaches new biotenside esters for use in the preparation of spontaneously dispersible concentrates containing therapeutic or cosmetically active substances (col. 1, lines 7-10). Eugster '691 teaches that cyclophosphamide may be combined with these esters. See Eugster '691 at column 11, lines 55-56. Eugster '691 also teaches that the sterol esters disclosed therein may be incorporated into conventional pharmaceutical preparations, together with customary excipients and/or diluents and stabilizers.

The Examiner states that "it would have been prima facie obvious for one of ordinary skill in the art to modify Battistini's tablet composition using the amounts for the ingredients in view of the teaching of Eugster '691. The reason is to obtain a stable film coated tablets of cyclophosphamide." The reason given by the Examiner

does not appear to be disclosed in any of the references and streams directly from the disclosure of the present application. Neither Battistini '149 nor Eugster '691 discuss stability of the compositions according to their teachings. Furthermore, compositions disclosed by Eugster '691 are different from the compositions disclosed by Battistini '149. Compositions of Eugster '691 are prepared using specific new biotenside esters and result in spontaneously dispersible concentrates. Clearly, the stability of such spontaneously dispersible concentrates, even if it was discussed in the Eugster '691 reference, would not be relevant to film coated tablets disclosed by Battistini '149. Therefore, the modification of the compositions disclosed Battistini '149 as proposed by the Examiner for the reasons provided by the Examiner is not warranted.

The Examiner states that "exclusion of preswollen starch does not impart patentable distinct [sic], since the prior art obtained the same results desired by applicants, i.e., a coated tablet containing phosphamide having excellent stability and bioviability". Applicants strongly disagree with this statement. First of all, exclusion of a claimed component, preswollen starch, should be motivated by the teachings of the cited references. No motivation is provided by either reference to modify the hypothetical tyrosine kinase/cyclophosphamide compositions of Battistini '149 to comprise the claimed binders exclusive of preswollen starch. Furthermore, as discussed above, neither one of the references address the stability characteristics of the disclosed compositions, much less any connection between the type of starch used and the stability of cyclophosphamides. It is the Applicants finding that exclusion of specific starches provides improved stability of the compositions containing phosphamides. At best, the references equate all types of starch as suitable fillers. Applicants have shown that exclusion of pre-swollen starch results in

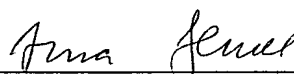
unexpectedly improved stability of cyclophosphamide and reduced discoloration of the disclosed compositions. See Table on page 3, especially examples 9 and 10.

These results could not have been expected from the teachings of the cited references alone or in combination. Thus, Battistini '149 in combination with Eugster '691 neither suggests nor renders obvious the claimed invention. Reconsideration and withdrawal of the rejection are respectfully requested.

In view of the foregoing amendments and remarks, Applicants respectfully submit that the application is in condition for allowance. Notification to that effect is respectfully requested. Should any questions relating to patentability remain, the Examiner is invited to telephone the undersigned to discuss the same.

Respectfully submitted,

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